

METHOD AND APPARATUS FOR FOURIER TRANSFORM MASS  
SPECTROMETRY (FTMS) IN A LINEAR MULTIPOLE ION TRAP

1 TECHNICAL FIELD OF THE INVENTION

2 The present invention relates generally to means and method  
3 for a linear, multipole ion trap whereby ions from an ion source  
4 are transmitted through a differential pump system and into a  
5 multipole trap device for trapping and analysis. More  
6 specifically, an apparatus for a linear quadrupole trap is  
7 described which uses one multipole device comprising two trapping  
8 regions and one analyzing section to provide an improved mass  
9 analyzer.

10  
11 BACKGROUND OF THE PRESENT INVENTION

12 The present invention relates generally to a multipole ion  
13 trap for use in mass spectrometry. The methods for transferring,  
14 trapping and analyzing ions described herein are enhancements of  
15 the techniques referred to in the literature relating to mass  
16 spectrometry.

17 Mass spectrometry is an important tool in the analysis of a  
18 wide range of chemical compounds. Specifically, mass spectrometers  
19 can be used to determine the molecular weight of sample compounds.

1 The analysis of samples by mass spectrometry consists of three main  
2 steps - formation of gas phase ions from sample material, mass  
3 analysis of the ions to separate the ions from one another  
4 according to ion mass, and detection of the ions. A variety of  
5 means exist in the field of mass spectrometry to perform each of  
6 these three functions. The particular combination of means used in  
7 a given spectrometer determine the characteristics of that  
8 spectrometer.

9 To mass analyze ions, for example, one might use a magnetic  
10 (B) or electrostatic (E) analyzer. Ions passing through a magnetic  
11 or electrostatic field will follow a curved path. In a magnetic  
12 field the curvature of the path will be indicative of the momentum-  
13 to-charge ratio of the ion. In an electrostatic field, the  
14 curvature of the path will be indicative of the energy-to-charge  
15 ratio of the ion. If magnetic and electrostatic analyzers are used  
16 consecutively, then both the momentum-to-charge and energy-to-  
17 charge ratios of the ions will be known and the mass of the ion  
18 will thereby be determined. Other mass analyzers are the  
19 quadrupole (Q), the ion cyclotron resonance (ICR), the time-of-  
20 flight (TOF), and the quadrupole ion trap analyzers.

21 Before mass analysis can begin, however, gas phase ions must

1 be formed from sample material. If the sample material is  
2 sufficiently volatile, ions may be formed by electron impact (EI)  
3 or chemical ionization (CI) of the gas phase sample molecules. For  
4 solid samples (e.g. semiconductors, or crystallized materials),  
5 ions can be formed by desorption and ionization of sample molecules  
6 by bombardment with high energy particles. Secondary ion mass  
7 spectrometry (SIMS), for example, uses keV ions to desorb and  
8 ionize sample material. In the SIMS process a large amount of  
9 energy is deposited in the analyte molecules. As a result, fragile  
10 molecules will be fragmented. This fragmentation is undesirable in  
11 that information regarding the original composition of the sample  
12 -- e.g., the molecular weight of sample molecules -- will be lost.

13 For more labile, fragile molecules, other ionization methods  
14 now exist. The plasma desorption (PD) technique was introduced by  
15 Macfarlane et al. in 1974 (Macfarlane, R. D.; Skowronski, R. P.;  
16 Torgerson, D. F., *Biochem. Biophys. Res Commun.* 60 (1974) 616).  
17 Macfarlane et al. discovered that the impact of high energy (MeV)  
18 ions on a surface, like SIMS would cause desorption and ionization  
19 of small analyte molecules, however, unlike SIMS, the PD process  
20 results also in the desorption of larger, more labile species --  
21 e.g., insulin and other protein molecules.

Lasers have been used in a similar manner to induce desorption of biological or other labile molecules. See, for example, VanBreeman, R.B.; Snow, M.; Cotter, R.J., *Int. J. Mass Spectrom. Ion Phys.* **49** (1983) 35; Tabet, J.C.; Cotter, R.J., *Anal. Chem.* **56** (1984) 1662; or Olthoff, J.K.; Lys, I.; Demirev, P.; Cotter, R. J., *Anal. Instrument.* **16** (1987) 93. Cotter et al. modified a CVC 2000 time-of-flight mass spectrometer for infrared laser desorption of involatile biomolecules, using a Tachisto (Needham, Mass.) model 215G pulsed carbon dioxide laser. The plasma or laser desorption and ionization of labile molecules relies on the deposition of little or no energy in the analyte molecules of interest. The use of lasers to desorb and ionize labile molecules intact was enhanced by the introduction of matrix assisted laser desorption ionization (MALDI) (Tanaka, K.; Waki, H.; Ido, Y.; Akita, S.; Yoshida, Y.; Yoshica, T., *Rapid Commun. Mass Spectrom.* **2** (1988) 151 and Karas, M.; Hillenkamp, F., *Anal. Chem.* **60** (1988) 2299). In the MALDI process, an analyte is dissolved in a solid, organic matrix. Laser light of a wavelength that is absorbed by the solid matrix but not by the analyte is used to excite the sample. Thus, the matrix is excited directly by the laser, and the excited matrix sublimates into the gas phase carrying with it the

1 analyte molecules. The analyte molecules are then ionized by  
2 proton, electron, or cation transfer from the matrix molecules to  
3 the analyte molecules. This process, MALDI, is typically used in  
4 conjunction with time-of-flight mass spectrometry (TOFMS) and can  
5 be used to measure the molecular weights of proteins in excess of  
6 100,000 daltons.

7 Atmospheric pressure ionization (API) includes a number of  
8 methods. Typically, analyte ions are produced from liquid solution  
9 at atmospheric pressure. One of the more widely used methods,  
10 known as electrospray ionization (ESI), was first suggested by Dole  
11 et al. (M. Dole, L.L. Mack, R.L. Hines, R.C. Mobley, L.D. Ferguson,  
12 M.B. Alice, *J. Chem. Phys.* **49**, 2240, 1968). In the electrospray  
13 technique, analyte is dissolved in a liquid solution and sprayed  
14 from a needle. The spray is induced by the application of a  
15 potential difference between the needle and a counter electrode.  
16 The spray results in the formation of fine, charged droplets of  
17 solution containing analyte molecules. In the gas phase, the  
18 solvent evaporates leaving behind charged, gas phase, analyte ions.  
19 Very large ions can be formed in this way. Ions as large as 1 MDa  
20 have been detected by ESI in conjunction with mass spectrometry  
21 (ESMS).

1 ESMS was introduced by Yamashita and Fenn (M. Yamashita and  
2 J.B. Fenn, *J. Phys. Chem.* **88**, 4671, 1984). To establish this  
3 combination of ESI and MS, ions had to be formed at atmospheric  
4 pressure, and then introduced into the vacuum system of a mass  
5 analyzer via a differentially pumped interface. The combination of  
6 ESI and MS afforded scientists the opportunity to mass analyze a  
7 wide range of samples. ESMS is now widely used primarily in the  
8 analysis of biomolecules (e.g. proteins) and complex organic  
9 molecules.

10 In the intervening years a number of means and methods useful  
11 to ESMS and API-MS have been developed. Specifically, much work  
12 has focused on sprayers and ionization chambers. In addition to  
13 the original electrospray technique, pneumatic assisted  
14 electrospray, dual electrospray, and nano electrospray are now also  
15 widely available. Pneumatic assisted electrospray (A.P. Bruins,  
16 T.R. Covey, and J.D. Henion, *Anal. Chem.* **59**, 2642, 1987) uses  
17 nebulizing gas flowing past the tip of the spray needle to assist  
18 in the formation of droplets. The nebulization gas assists in the  
19 formation of the spray and thereby makes the operation of the ESI  
20 easier. Nano electrospray (M.S. Wilm, M. Mann, *Int. J. Mass*  
21 *Spectrom. Ion Processes* **136**, 167, 1994) employs a much smaller

1 diameter needle than the original electrospray. As a result the  
2 flow rate of sample to the tip is lower and the droplets in the  
3 spray are finer. However, the ion signal provided by nano  
4 electrospray in conjunction with MS is essentially the same as with  
5 the original electrospray. Nano electrospray is therefore much  
6 more sensitive with respect to the amount of material necessary to  
7 perform a given analysis.

8 In the field of Fourier Transform ion cyclotron Resonance Mass  
9 Spectrometry ("FTICR-MS") a Penning ion Trap is used to trap ions.  
10 The conventional Penning trap consists of six metal plates forming  
11 a cube in a magnetic field (M.B. Comisarow, *Adv. Mass Spectrom.* 8,  
12 1698(1980), M.B. Comisarow, *Int. J. Mass Spectrom. Ion Phys.* 37,  
13 251(1981)). Two of these plates ("trapping plates") reside in  
14 planes perpendicular to the magnetic field whereas the other four  
15 plates are in planes parallel to the magnetic field. In  
16 conventional FTICR-MS, the trapping plates together with the  
17 magnetic field are used to trap ions. This is accomplished by  
18 applying a small electrical potential (e.g. 1V) to the trapping  
19 plates. The remaining plates are held at ground potential. The  
20 magnetic field confines ions in the plane perpendicular to the  
21 magnetic field line, and the electric field produced by the

1 potential difference between the trap electrodes confines the ions  
2 along the magnetic field lines.

3 Ions in a uniform magnetic field, barring other influences,  
4 move in circular orbits (cyclotron motion) with a frequency  
5 proportional to ion mass-to-charge ratio (A.G. Marshall, L.H.  
6 Christopher, G.S. Jackson, *Mass Spectrom. Rev.*, in press, 1998).

7 However, the presence of an electrostatic field, such as that  
8 produced by the trapping plates, produces new modes of motion  
9 (magnetron, and trapping) and alters the frequency of the cyclotron  
10 motion of the ions. This reduces the resolution of the  
11 spectrometer and causes a distortion in the relationship between  
12 ion  $m/z$  and cyclotron frequency.

13 The magnitude of the potentials placed on the trapping  
14 electrodes is significant both to the degree to which the cyclotron  
15 motion is distorted and to the range of the kinetic energy that an  
16 ion can have along the magnetic field lines and still be trapped.  
17 The kinetic energy of the ions which can be trapped is directly  
18 related to the potential on the trapping electrodes and so is the  
19 distortion on the cyclotron motion. Thus, in a prior art FTICR  
20 cell, the potential on the trapping electrodes would be set as a  
21 compromise between trapable ion kinetic energy and distortion in



1 cyclotron motion. The trapping potential must be kept low (e.g.  
2 1V) to avoid excessive cyclotron motion, and as a result, the range  
3 of trapable ion kinetic energies is also low (e.g. 1 eV). This  
4 limits the FTMS method in its application to external ion sources  
5 because such sources often produce ion beams which have a broad  
6 range of kinetic energies (R.C. Beavis, B.T. Chait, *Chem. Phy.*  
7 *Lett.* **181**, 479(1991), T.-W.D. Chan et al., *Chem. Phy. Lett.* **222**,  
8 579(1994), J.A. Castoro, C. Koester, C.L. Wilkins, *Rapid Commun.*  
9 *Mass Spectrom.* **6**, 239(1992), C. Koester, J.A. Castoro, C.L.  
10 Wilkins, *J. Am. Chem. Soc.* **114**, 7572(1992), J. Yao, M.Dey, S.J.  
11 Pastor, C.L. Wilkins, *Anal. Chem.* **67**, 3638(1995), T. Solouki, D.H.  
12 Russel, *Proc. Natl. Acad. Sci. USA* **89**, 5701(1992), T. Solouki, K.J.  
13 Gilling, D.H. Russel, *Anal. Chem.* **66**, 1583(1994)).

14 In Laude et al. ("Laude"), cylindrical compensation electrodes  
15 were inserted between the trap electrodes and the excite/detect  
16 electrodes (V.H. Vartanian, F. Hadjarab, D.A. laude, *Int. J. Mass*  
17 *Spectrom. Ion Proc.* **151**, 157(1995)). A reduction in the cyclotron  
18 frequency shift of more than 99% was observed.

19 In the related field of quadrupole mass spectrometry, ions are  
20 analyzed via an oscillating electric field ("Quadrupole Mass  
21 Spectrometry and its Applications", Peter Dawson, ed., copyright

1 1976, Elsevier Publishing Company, Amsterdam). Typically a  
2 quadrupolar electric field is established between four electrodes  
3 in the case of a linear quadrupole. Ions are injected into one end  
4 of the linear quadrupole and under the influence of the electric  
5 field, either pass through to the exit end of the quadrupole or are  
6 caused to collide with the electrodes of the quadrupole. By  
7 applying the appropriate static and oscillating potentials between  
8 the electrodes of the quadrupole, one can select ions of a  
9 prespecified mass-to-charge ratio ( $m/z$ ) to pass from the entrance  
10 of the quadrupole to its exit while largely excluding all other  $m/z$   
11 ions. Thus, the device acts as a quadrupole mass filter.

12 The electrodes of a quadrupole mass filter might be designed  
13 in many ways. Ideally, four electrodes each having a hyperbolic  
14 surface can be used. In theory, electrodes of this form could be  
15 used to produce a perfectly quadrupolar electric field. In  
16 practice, electrodes of cylindrical geometry are typically used.  
17 That is, four cylindrical, rod shaped electrodes are placed  
18 symmetrically about the axis of the quadrupole mass filter. This  
19 arrangement of electrodes is easier to produce than the hyperbolic  
20 electrodes and can be used to produce a close approximation of a  
21 quadrupolar electric field.

1           Alternatively, researchers such as T. Hayashi and N. Sakudo  
2           (T. Hayashi and N. Sakudo, Proc. Int. Conf. Mass Spectrom., Hyoto,  
3           Japan, 1969 ("Hayashi and Sakudo")), and more recently J. Prestage  
4           (John D. Prestage, *NASA Technical Brief* 23(5), pp. 168 (May 1999)  
5           ("Prestage")) have employed arch shaped electrodes to produce  
6           quadrupole mass filters. Such electrode arrangements might also be  
7           used to produce close approximations of quadrupolar electric  
8           fields. More than four electrodes may be used in such designs. A  
9           larger number of electrodes allows for a closer approximation of a  
10          quadrupolar field. For example, by employing eight electrodes,  
11          Prestage can approximate the quadrupolar field to sixth order.  
12          Advantages of this method of producing a quadrupole mass filter  
13          include relatively easy production, light weight construction, and  
14          less power consumed during operation.

15          For Example, FIG. 1 depicts the multipole ion guide of  
16          Prestage. Shown is multipole ion guide 6 comprising eight  
17          electrodes 2 & 4 are arranged symmetrically around a central axis.  
18          Four electrodes 2 are grounded, while an oscillating potential of  
19           $\pm V$  is applied between the remaining four electrodes 4. The  
20          multipole is extended along its axis and cylindrical in shape with  
21          two openings for ions to enter 8 and exit 10 the guide 6. When used

1 as a quadrupole mass filter, the ions enter the guide, and selected  
2 ions pass through the device to the exit end 10. To be mass  
3 selective, a DC potential is applied between the V+ electrodes and  
4 the V- electrodes. If no DC potential is applied, the device will  
5 simply transfer ions from the entrance 8 to the exit end 10 of the  
6 device.

7 An alternate embodiment of the multipole 6 of Prestage is  
8 depicted in FIG. 2. In addition to the multipole of FIG. 1, there  
9 are two cylindrically symmetric apertured plates 12 & 14. The  
10 apertured plates 12 & 14 are disposed on opposite ends of the  
11 multipole. The first apertured plate 14, labeled the "Entrance  
12 Electrode" is between the ion source(not shown) the entrance 8.  
13 The second apertured plate 12 is disposed downstream the first  
14 plate 14 and it is labeled the "Exit Electrode". By applying a DC  
15 offset between these electrodes and the multipole, ions can be  
16 trapped in the multipole. Ions would be contained radially by the  
17 RF potential applied between the +/- V electrodes and axially by  
18 the potential applied to the entrance and exit electrodes.

19 A second form of quadrupole mass analyzer is referred to as a  
20 quadrupole ion trap (or Paul trap). In contrast to the Penning  
21 trap of FTICR MS, the Paul trap does not require and does not use

1 a magnetic field to trap ions. Rather, only an oscillating  
2 electric field is used to trap the ions. The Paul trap is a  
3 cylindrically symmetric trap composed of three electrodes - a  
4 central "ring" electrode and two "cap" electrodes. The two cap  
5 electrodes are typically held at the same electrical potential. An  
6 oscillating electric field is applied between the cap electrodes  
7 and the ring-electrode to form a three dimensional quadrupolar  
8 field in the interior of the device. Ions can be trapped and  
9 manipulated in a variety of ways in this electric field.

10 Within a quadrupolar electric field, either in a linear device  
11 or a three dimensional trap, ions will oscillate with a frequency  
12 of motion dependent only on the  $m/z$  of the ion. In prior art  
13 quadrupole mass analyzers, this characteristic frequency has been  
14 used to select, excite, and eject ions from the quadrupole device.  
15 In contrast to FTICR MS, ions are detected via a "channeltron"- or  
16 other similar- detector rather than by inductive detection. The  
17 ions collide with the detector, and are destroyed in the detection  
18 process. The inductive detection of FTICR MS preserves the ions  
19 because the ions do not collide with the detection device during  
20 the detection process.

21 A third type of related mass analyzer utilizes the Kingdon

1 trap (R.D. Knight, *Appl. Phys. Lett.* 38(4), 221 (1981)). As  
 2 suggested by R.D. Knight and later by A. Makarov, the Kingdon trap  
 3 can be used to trap ions and analyze ions in a one dimensional  
 4 quadratic electrostatic field. In this case, a central electrode  
 5 and two "outer" electrodes are used to generate a cylindrically  
 6 symmetric electrostatic field of the form:

$$F = -A (Z^2 - r^2/2 + B \ln r)$$

8 Where F is the electric potential, r is the distance from the axis  
 9 of the trap, z is the position along the axis of the device, and A  
 10 and B are constants. Clearly from this equation, the field along  
 11 the axis of the trap is quadratic. Thus, ions will oscillate along  
 12 this axis with a periodic frequency directly related to the mass-  
 13 to-charge ratio of the ion. The two outer electrodes are placed  
 14 opposite one another along the axis of the trap such that the ions  
 15 oscillate between them with the above mentioned periodic motion.  
 16 As in the FTICR, ions can be detected via their induced charge on  
 17 the outer electrodes (A. Makarov, Proceedings of the 47<sup>th</sup> ASMS  
 18 Conference on Mass Spectrometry and Allied Topics, 2828(1999)).

19 Yet another quadrupole ion trap has been disclosed by Micheal  
 20 W. Senko, Jae C. Schwartz, Alan E. Schoen and John E.P. Syka,  
 21 Proceedings of the 48<sup>th</sup> ASMS Conference on Mass Spectrometry and

1 Allied Topics, June 11-15, 2000. Senko et al. disclose a linear  
2 quadrupole ion trap comprising a symmetrical arrangement of four  
3 detection electrodes and four RF trapping electrodes equally spaced  
4 apart around a central longitudinal axis. In the design of Senko  
5 et al., each detection electrode is positioned between two RF  
6 trapping electrodes, and each RF trapping electrode is positioned  
7 between two detection electrodes. Importantly, the electrodes  
8 (both detection and trapping) in the Senko et al. design are spaced  
9 apart from each other. Such design results in undesirable feedback  
10 due to capacitive mismatches as well as RF imbalances.

11 According to Senko et al., having a truly symmetrically  
12 designed quadrupole ion trap will eliminate all feedback detected  
13 by the detector from the RF trapping field. This, of course, would  
14 require the system be constructed such that it is capacitively  
15 matched and that the system be perfectly RF balanced. However, the  
16 Senko et al. design is not perfectly RF balanced nor is it  
17 capacitively matched. One way Senko et al. attempt to overcome  
18 this is by employing high voltage capacitors between each detection  
19 and trapping electrode of the system. This too fails to eliminate  
20 all of the feedback.

21 Each of the prior art trapping mass analyzers described above

1 has certain advantages and disadvantages. First, for example,  
2 advantages of the FTICR mass spectrometer include high resolution,  
3 and mass accuracy, the ability to select ions and perform tandem  
4 mass spectrometry (i.e. the selection of ions based on  $m/z$ , the  
5 fragmentation of the selected ions, and the mass analysis of the  
6 fragment ions) on those ions, to detect ions non-destructively, and  
7 to detect ions simultaneously across a wide  $m/z$  range. Conversely,  
8 disadvantages of FTICR include the required use of a strong, highly  
9 homogeneous magnetic field, a limited mass range, and limited speed  
10 of mass analysis. Second, advantages of the quadrupole mass filter  
11 include relative ease of production and use, sensitivity, and  
12 quantitation while, disadvantages of the quadrupole mass filter  
13 include limited mass range, speed of mass analysis, mass accuracy,  
14 and mass resolution. Third, advantages of the alternate design  
15 quadrupole mass filters (e.g. as given by Prestage) are potentially  
16 further simplified production, lighter weight, and lower power  
17 consumed. While disadvantages are lower resolution, mass accuracy,  
18 general performance (i.e. the field produced in such a device is  
19 not truly quadratic). Fourth advantages of the quadrupole ion trap  
20 are the ability to trap and select ions to perform tandem mass  
21 spectrometry experiments on the trapped ions, moderate resolution,



1 and moderate mass accuracy. Disadvantages of the quadrupole ion  
2 trap are the dependence of mass resolution on scan speed, poor duty  
3 cycle (i.e. most ions are lost rather than analyzed, poor trapping  
4 capacity) only a small number of ions can be trapped without  
5 perturbing the mass analysis. Fifth, advantages of the Kingdon  
6 trap are the ability to trap and analyze ions without the need for  
7 a magnetic field (as in FTICR) and without the need for an  
8 oscillating electrical potential (as used with quadrupole mass  
9 filters and quadrupole traps), the ability to detect ions non-  
10 destructively, moderate mass resolving power, and potentially the  
11 ability to perform tandem mass spectrometry experiments. On the  
12 other hand, disadvantages of the Kingdon trap are difficulty of  
13 forming and aligning the trap electrodes, complexity of ion  
14 introduction into the trap (i.e. ions are trapped only so long as  
15 they have a stable orbit about the central electrode) difficulty to  
16 excite ions into a coherent axial motion. Yet another disadvantage  
17 of the prior art designs includes the existence of undesirable  
18 feedback.

19 The present invention distinguishes itself from prior art by  
20 providing a means and method for a novel type of mass analyzer  
21 having a unique set of advantages over the above mentioned mass

1 analyzers.

2  
3 SUMMARY OF THE INVENTION

4 The present invention provides a means and method for a new  
5 type of mass analyzer capable of filtering and trapping ions with  
6 specific advantages over prior art mass analyzers.

7 In the prior art multipole design according to Prestage (FIGS.  
8 1 and 2), eight electrodes are arranged symmetrically around a  
9 central axis. Four of these are grounded and an oscillating  
10 potential of  $\pm V$  is applied between the other four electrodes.  
11 According to Prestage, the multipole is extended along its axis  
12 such that it is substantially cylindrical in shape. Being  
13 cylindrical, the device has two openings, -- one at each end -- and  
14 the device can be used as a quadrupole mass filter. In this case,  
15 ions enter one end of the multipole and only selected ions pass  
16 completely through the multipole to its exit end. If the multipole  
17 is to be mass selective, then a DC potential must be applied  
18 between the  $V+$  electrodes and the  $V-$  electrodes. Alternatively, if  
19 no DC potential is applied, the multipole may be used as an ion  
20 guide (i.e., simply to transfer ions from the entrance end to the  
21 exit end of the device).

1 According to the present invention, the electrodes which were  
2 grounded according to Prestage are held only nominally at 0 volts.  
3 For example, these electrodes are each independently connected to  
4 ground through a 1 megaohm (Mohm) resistor. These nominally  
5 grounded electrodes are then used to detect trapped ions via charge  
6 induction in the manner of Fourier Transform Ion Cyclotron  
7 Resonance (FTICR) Mass Spectrometer. More particularly, ions are  
8 first cooled to the center of the trap via collisions with the rest  
9 gas. During subsequent ion excitation and detection, the trap is  
10 substantially free of gas. The ions are then excited by applying  
11 a broadband excitation pulse between the V+ and V- electrodes.  
12 This broadband excitation pulse is applied so as to induce the ions  
13 to orbit about the axis of the ion trap in coherent ion packets.  
14 While ions might be distributed along the length of the trap,  
15 substantially all ions of a given m/z should be at about the same  
16 angular position in their orbits at the same time. Further, ions  
17 of a given m/z will have a given frequency of motion about the  
18 central axis of the trap. As in conventional FTICR, by measuring  
19 the frequency of the signal induced on the detection electrodes,  
20 the m/z of the ions can be determined, and by measuring the  
21 amplitude of the induced signal, the relative number of ions of

1 that given  $m/z$  can be determined.

2 In an alternate embodiment of the linear multipole trap  
3 according to the present invention, a central set of electrodes and  
4 two trapping electrodes (instead of the DC trap electrodes) may be  
5 used. The trapping multipoles are held at a slightly higher DC  
6 potential than the central analysis multipole (e.g., 2V). This DC  
7 offset between the multipoles serves to trap ions in the analysis  
8 multipole (i.e., the central electrodes). At the ends of the  
9 analysis multipole, the oscillating quadrupolar field is not  
10 greatly perturbed and therefore the motion of the ions at the  
11 center of the multipole is therefore substantially the same as the  
12 motion of ions near the ends of the analysis multipole. The RF  
13 electrodes of the trapping multipoles and analysis multipoles are  
14 all driven by the same RF driver. Therefore, the RF electrodes  
15 will all have the same potentials and frequencies applied to them,  
16 and the RF electrodes of the analyzing multipole are capacitively  
17 coupled to their counterparts in the trapping multipoles.

18 Yet another embodiment of the linear multipole trap according  
19 to the invention may comprise only a single multipole with the  
20 detection electrodes divided into three sections to achieve the  
21 same effect. That is, the central section is the "analyzing"

1 section, whereas the two outer sections are the "trapping"  
2 sections. The regions of the detection electrodes defining the  
3 trapping section of the multipole are not used to detect ions --  
4 rather, these electrodes are held at a high DC potential with  
5 respect to the central detection electrodes, which tends to repel  
6 the ions back into the analyzing section. The combination of this  
7 DC field and the RF field generated by the potential applied  
8 between the RF electrodes, traps ions within the analyzing section  
9 of the multipole. The advantage of this embodiment is that,  
10 without regard to mechanical tolerances, the RF field is guaranteed  
11 to be homogeneous throughout the multipole (i.e., there is no RF  
12 electric field component along the axis of multipole and the RF  
13 field experienced by an ion is not dependent on its position along  
14 the axis of the multipole).

15 In a mass spectrometer employing the preferred embodiment of  
16 the linear multipole trap according to the present invention, ions  
17 may be generated at an elevated pressure (e.g., atmospheric  
18 pressure) via, for example, electrospray ionization. Ions are  
19 transferred, by entrainment in a gas flow, through a capillary from  
20 the atmospheric pressure region into a first pumping region. Some  
21 of these ions pass through the first pumping region and into a

1 second pumping region through a skimmer. In the second pumping  
2 region, ions enter a first trapping section of the multipole. The  
3 pressure in the second pumping region is such that ions undergo  
4 sufficient collisions with the gas in the first trapping section of  
5 the linear multipole trap to be cooled to near room temperature  
6 (e.g.,  $10^{-2}$  mbar). Having been cooled to near room temperature, the  
7 ions are allowed to pass into the analysis section. This third  
8 pumping region is pumped to a lower pressure than the second  
9 pumping region, such that the ions have a large mean free path.

10 Other objects, features, and characteristics of the present  
11 invention, as well as the methods of operation and functions of the  
12 related elements of the structure, and the combination of parts and  
13 economies of manufacture, will become more apparent upon  
14 consideration of the following detailed description with reference  
15 to the accompanying drawings, all of which form a part of this  
16 specification.

#### 17 18 BRIEF DESCRIPTION OF THE DRAWINGS

19 A further understanding of the present invention can be  
20 obtained by reference to a preferred embodiment set forth in the  
21 illustrations of the accompanying drawings. Although the

1 illustrated embodiment is merely exemplary of systems for carrying  
2 out the present invention, both the organization and method of  
3 operation of the invention, in general, together with further  
4 objectives and advantages thereof, may be more easily understood by  
5 reference to the drawings and the following description. The  
6 drawings are not intended to limit the scope of this invention,  
7 which is set forth with particularity in the claims as appended or  
8 as subsequently amended, but merely to clarify and exemplify the  
9 invention.

10 For a more complete understanding of the present invention,  
11 reference is now made to the following drawings in which:

12 FIG. 1 shows a prior art multipole design according to J. D.  
13 Prestage with eight electrodes arranged symmetrically around a  
14 central axis;

15 FIG. 2 shows the prior art multipole design of FIG. 1 further  
16 comprising cylindrically symmetric apertured plates at either end  
17 thereof;

18 FIG. 3 shows the preferred embodiment of the linear quadrupole  
19 trap according to the present invention having DC trap electrodes;

20 FIG. 4 shows an alternate embodiment of the linear quadrupole  
21 trap according to the present invention, having a central set of

1 electrodes;

2 FIG. 5 shows another alternate embodiment of the linear  
3 quadrupole trap according to the present invention, comprising a  
4 single multipole having a single set of RF electrodes;

5 FIG. 6 shows the linear quadrupole trap of FIG. 5 as it may be  
6 implemented into a mass spectrometer for performing tandem mass  
7 spectrometry analysis.

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DETAILED DESCRIPTION OF A PREFERRED EMBODIMENT

As required, a detailed illustrative embodiment of the  
present invention is disclosed herein. However, techniques,  
systems and operating structures in accordance with the present  
invention may be embodied in a wide variety of forms and modes,  
some of which may be quite different from those in the disclosed  
embodiment. Consequently, the specific structural and functional  
details disclosed herein are merely representative, yet in that  
regard, they are deemed to afford the best embodiment for  
purposes of disclosure and to provide a basis for the claims  
herein which define the scope of the present invention. The  
following presents a detailed description of a preferred  
embodiment (as well as some alternative embodiments) of the



1 present invention.

2 Referring first to FIG. 3, depicted is a multipole ion  
3 guide, similar to the Prestage device of FIG. 2, with the  
4 grounded electrodes 16 only nominally held at zero volts. In  
5 contrast, each electrode 16 of multipole device 20 is connected  
6 to ground (e.g, independently through a 1Mohm resistor).  
7 Electrodes 16 & 18 detect trapped ions by charge induction in the  
8 manner of FTICR mass spectrometry. The ions are first cooled to  
9 the center-line of the trap 20 by collisions with a rest gas at a  
10 pressure in the range of about  $10^{-2}$  to  $10^{-3}$  mbar. Next, the gas  
11 is pumped away such that the ion trap 20 is operated in a vacuum  
12 at a pressure in the range of about  $10^{-7}$  to  $10^{-10}$  mbar. The +/- V  
13 electrodes 18 generates a broadband excitation pulse and gives  
14 the ions a velocity in a direction perpendicular to the axis of  
15 the trap 20. The ions then orbit the axis of the ion trap 20 in  
16 coherent ion packets with ions of a given m/z at about the same  
17 angular position in their orbits at the same time. The frequency  
18 of the motion of ions of a given m/z about the axis of the trap  
19 20 can be measured by the signal induced on the detection  
20 electrodes. Also, the four nominally grounded electrodes 16 are  
21 divided into two "Detect" 16a electrodes that are electrically

1 connected, and two "Detect'" 16b electrodes that are also  
2 electrically connected, respectively. The Detect 16a electrodes  
3 and the Detect' 16b electrodes are connected to two respective  
4 inputs of a differential amplifier. As a result, for every orbit  
5 of the ions, two cycles are detected in the induced signal.

6 Referring next to FIG. 4, depicted is the multipole 20 of  
7 FIG. 3-as it is incorporated between two trapping multipoles 22 &  
8 24. The trapping multipoles 22 & 24 are held at a higher DC  
9 potential than the central multipole 20. This arrangement allows  
10 for a more homogeneous quadrupolar field within the analysis  
11 multipole 20 and the ions at the center and at the ends of the  
12 multipole 10 will have the same motion. All of the RF electrodes  
13 18a, 18b & 18c of the trapping multipoles and the analyzing  
14 multipoles will have the same potentials and frequencies.  
15 Therefore, RF electrodes 18a are capacitively coupled to 18b and  
16 18c.

17 Turning now to FIG. 5, depicted is a single multipole 26  
18 with a single set of RF electrodes 28, and detection electrodes  
19 30 divided into three sections. The divisions made by the  
20 detection electrodes 30 define the trapping sections 32 & 36, and  
21 the analyzing section 34. The detection electrodes 30 in the

1 trapping sections 32 & 36 are held at a DC potential (e.g., in  
2 the range from 0.1 volts to 100 volts) with respect to the  
3 central detection electrodes 30 to trap ions in the central  
4 analyzing region 34. The detection electrodes 30b & 30c in the  
5 two trapping regions 32 & 34 are not used for detection.  
6 Instead, these electrodes 30b & 30c are held at a DC potential  
7 with respect to the central detection electrodes 30a. In this  
8 embodiment, the RF field generated by the RF electrodes 28 may be  
9 substantially homogeneous within the multipole.

10 Finally, referring to FIG. 6, depicted is a mass  
11 spectrometer employing the preferred embodiment of the linear  
12 multipole trap of FIG. 5 using an atmospheric pressure ion source  
13 38. The ions are transferred by gas flow through a capillary 40  
14 into a first differential pumping region 42 from an elevated  
15 pressure source 56. Some ions then pass into a second  
16 differential pumping region through a skimmer 44. The ions then  
17 enter the first trapping multipole 60 of the multipole device 54.  
18 The pressure of the second pumping region 56 allows the gas of  
19 the first trapping section 60 to cool the ions to near room  
20 temperature. Ions are then allowed to enter the central  
21 analyzing region 62 of the multipole 54 within a third pumping

1 region 54. Before reaching the analysis section, the ions move  
2 into yet a third pumping region, which is separated from the  
3 second pumping region by a pumping restriction. The third  
4 pumping region 54 is at a lower pressure than the second pumping  
5 region 56 to produce a higher resolution mass spectrum. This is  
6 important for producing long transients during ion detection and  
7 therefore a higher resolution mass spectrum. Once the ions are  
8 in the analysis section, a DC potential is applied to the DC  
9 electrodes of the first trapping section such that ions become  
10 trapped in the analysis section of the linear multipole trap  
11 through the combination of the RF and DC fields between the  
12 electrodes. Optionally, the trapping potential on the DC  
13 electrodes of the second trapping section may be kept on  
14 continuously.

15 In the analysis region 62, a DC potential is applied to the  
16 DC electrodes 68 of the first trapping section 60 to stop the  
17 ions from escaping the analysis region 62. Again, ions are  
18 excited into periodic motion by an electrical pulse applied  
19 between either the RF 64 or DC electrodes 66, 68 & 70. After the  
20 excitation pulse is turned off, the ions are detected by charge  
21 induction on the detection electrodes 66. Using the apparatus of

figure 6, tandem mass spectrometry experiments may be formed.

During analysis, ions are excited into periodic motion by an electrical pulse applied between either the RF or DC electrodes. After ion excitation, the excitation pulse is turned off and the ions are detected by charge induction on the detection electrodes. As excited ions orbit -- in a substantially circular orbit -- around the axis of the multipole, they approach each detection electrode in succession as a function of the ion's and electrodes' angular position. As discussed above, the detection electrodes are connected to a differential amplifier such that the potential on the detect electrode (i.e., the electrode nearest the ion being detected) is measured with respect to the potential on the detect' electrodes. This results in a substantially sinusoidal signal having a frequency corresponding to twice the orbital frequency of the ions and an amplitude proportional to the number of ions in the linear multipole trap.

Alternatively, the ions might be excited into a strongly oval orbit, approaching a periodic motion along a single axis of the multipole. In this case, the two detect electrodes are not electrically connected to one another (as suggested above), nor are the two detect' electrodes electrically connected to one another

1 (also as suggested above). The ions are excited into motion by  
2 applying an electrical pulse between, for example, the two detect'  
3 electrodes. The ions then will move back and forth substantially  
4 between these two detect' electrodes with little or no motion along  
5 the axis connecting the two detect electrodes. Once the ions are  
6 excited, the detect' electrodes are electronically switched from  
7 ~~excite mode to detect mode~~. In detect mode, the ions induce charge  
8 on the detect' electrodes. The opposing detect' electrodes are  
9 each electrically connected to one input of a differential  
10 amplifier. As above, the differential amplifier measures the  
11 potential difference between the opposing detect' electrodes. The  
12 result is (as described above) a substantially sinusoidal signal,  
13 the frequency of which corresponds to the frequency of the motion  
14 of ions between the two detect' electrodes and the amplitude of  
15 which is proportional to the number of ions in the trap.

16 Notice that the ions, once excited, will undergo oscillations  
17 for some extended period of time. This oscillation period is  
18 dependent on the pressure in the analyzer section of the multipole.  
19 If the pressure is sufficiently low (e.g.  $<10^{-9}$  mbar) the ions may  
20 oscillate for seconds. This will result in higher mass resolution  
21 and higher sensitivity in the mass spectrum produced.

1        It may happen that, due to micromotion (or some other cause),  
2        the phase of the ions may change during the analysis. Once the  
3        ions are sufficiently out of phase with one another, the signal  
4        induced on the detection electrodes by the ions will be low or non-  
5        existent. In such a case it may be desirable to cool the ions and  
6        reexcite them to perform a new measurement. According to the  
7        preferred embodiment of the invention this might be done by either  
8        pulsing gas into the analyzer section of the multipole to cool the  
9        ions to the center of the multipole, or by bringing the DC  
10        electrodes of the first trapping section to a neutral or attractive  
11        potential. By doing this, ions from the analyzer section would  
12        reenter the first trapping section (where the pressure is higher)  
13        and undergo collisional cooling via the gas in the first trapping  
14        region. Following this, ions could be reinjected into the analyzer  
15        section for repeated mass analysis. In a similar manner, one  
16        might perform tandem mass spectrometry experiments. In such a case  
17        all ions except those having the  $m/z$  of the precursor ion of  
18        interest are ejected from the analyzer section by, for example  
19        resonance ejection. Precursor ions might be accumulated for an  
20        extended period of time in the analyzer section so as to achieve a  
21        desired ion population. The precursor ions are then injected back

1 into first trapping section via a substantial potential on the DC  
2 electrodes of the first trapping section. This potential  
3 accelerates the ions to a "high" kinetic energy (e.g. 100 eV) such  
4 that when these ions collide with gas molecules in the multipole,  
5 they undergo fragmentation. The fragment ions formed in this way  
6 as well as the precursor ions are cooled to near room temperature  
7 by further collisions with the gas and then reinjected into the  
8 analysis section for mass analysis. Note that a new precursor  
9 might be selected from the fragment ion population for additional  
10 fragmentation and mass analysis. This process might be repeated  
11 many times in the performance of so called "MS<sup>n</sup>" experiments. Note  
12 also that after accumulating precursor ions above and before  
13 injecting the precursor ions into the first trapping section, it is  
14 necessary that additional ions be prevented from entering the  
15 multipole from the ion production region. To accomplish this a  
16 physical shutter might be used to block the passage of ions from  
17 the spray chamber to the multipole or a reverse bias might be  
18 applied between the exit of the transfer capillary and skimmer to  
19 repel ions from the skimmer so they do not pass the skimmer and get  
20 into the multipole.

21 Any other method used in the field of FTICR MS or quadrupole



1 or quadrupole trap MS - resonant ejection or isolation, IRMPD, SID,  
2 CID, SWIFT, BIRD, etc. - might be used in conjunction with the  
3 present invention.

4 While the present invention has been described with reference  
5 to one or more preferred embodiments, such embodiments are merely  
6 exemplary and are not intended to be limiting or represent an  
7 exhaustive enumeration of all aspects of the invention. The scope  
8 of the invention, therefore, shall be defined solely by the  
9 following claims. Further, it will be apparent to those of skill  
10 in the art that numerous changes may be made in such details  
11 without departing from the spirit and the principles of the  
12 invention. It should be appreciated that the present invention is  
13 capable of being embodied in other forms without departing from its  
14 essential characteristics.